Screening for Beryllium Sensitization Among Former Hanford Workers

T Takaro *, K Ertell *, L Newman [t], B Stover *, R Ponce,
E Faustman, T Kavanagh, S Barnhart *

CRESP-University of Washington
*University of Washington Occupational& Environmental Medicine Program
[t]Occupational/Environmental Medicine, National Jewish Center for Allergy & Immunology, Denver, CO

Consortium for Risk Evaluation with Stakeholder Participation, CRESP

Introduction

Workers at Hanford have been exposed to beryllium during fuel fabrication and research activities at the Hanford site. The extent of the exposure and resulting health outcomes are unknown, because worker exposures were not well characterized (many area samples but few personal samples) and past surveillance for beryllium health effects was not comprehensive and did not use sensitive monitoring tests.

.

Purpose of Pilot Study

- Determine the prevalence of sensitization in an exposed population of former Hanford workers
- Determine the high risk jobs of former workers and high risk areas for remediation
- Compare two different assay methods for the measurement of lymphocyte proliferation
- Begin medical monitoring for former workers at risk

Methods: Identifying Workers at Risk

Using several Hanford databases which contain information on worker identity, job history, building assignment, and beryllium exposure, **2482** workers have been identified as having worked in buildings where beryllium was used or as being in a prior beryllium medical surveillance program.

History of Beryllium Use at Hanford

- **Fuel Fabrication and Fuels Research Area (1955-1989)**

  Highest exposures expected in buildings 313 and 333
  Also buildings 306, 308, 326, 3706, 3712, 3720

- **Various R&D, machining/polishing operations (1950s - 1980s)**

  Buildings 231Z, 272W, 324, 325, 327, 329, 202S, others

Study Methods

- Locate former workers and confirm identity
- Mail information sheet, consent form, and medical/exposure questionnaire
- Upon completion of questionnaire and consent, workers are referred to local laboratory for BeLPT blood draw, then notified of results
- Positive responses to BeLPT are repeated and referred for medical evaluation if second test positive
- Analyze data

Methods: Population

- **Initial list**: former workers from Flow Gemini 698
  - Be screening program or buildings: 313, 333, 306, 326.
- **Industrial Hygiene:** paper records indicating work history 163
  - Building 313 or 333 and not in previous list.
- **Call In List:** workers who contacted us 49
  - Not in previous lists.
- **Building 5** list from Flow Gemini and REX 1572
  - work history data and not in previous lists.
  - Buildings 333,326,308,306 during years of beryllium operations

_____

- **Combined File** 2482
- Current workers are included in this list.

Methods: Medical Evaluation

- Lymphocyte proliferation testing by two different methods at a single point in time
  - Tritiated Thymidine Method (standard method)
  - Brd-Hoechst Method (newer, requires less blood, potentially more sensitive)
- Review of archived chest radiographs and spirometry for correlation with beryllium sensitization

Methods:Analysis

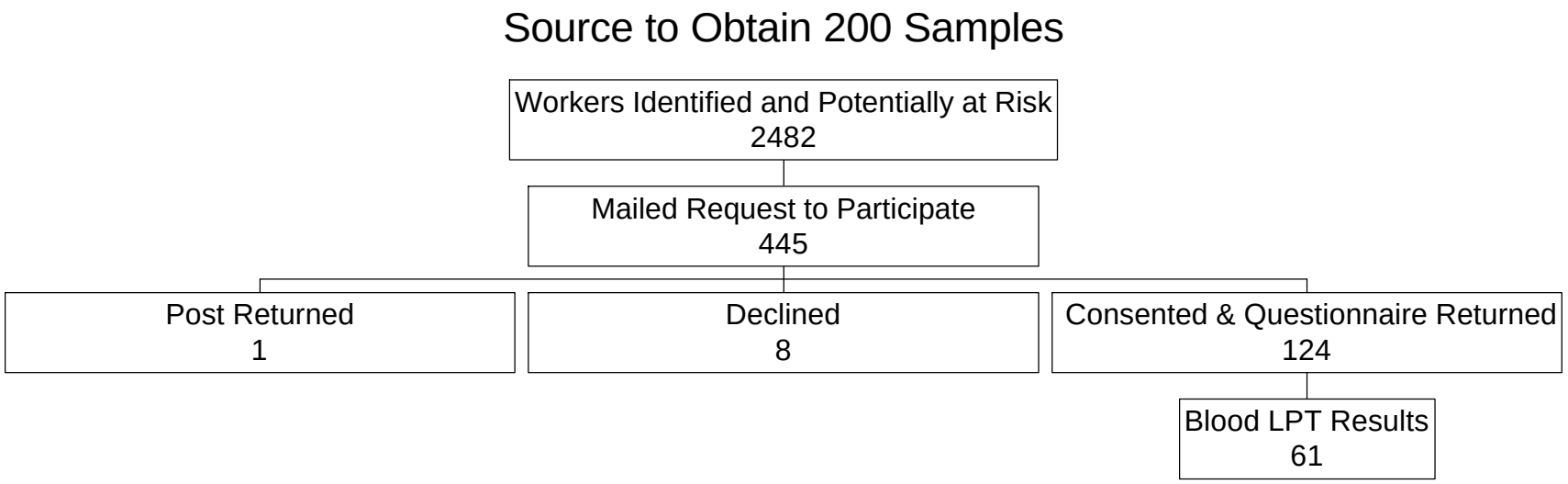
Prevalence rates for the following endpoints will be determined for participants:

- Beryllium sensitization by LPT
- Chest x-ray reticulo-nodular pattern (ILO>0/1)
- Spirometry showing restrictive or mixed disease

Regression Modeling will be used to evaluate high risk buildings and job tasks

Proliferation assays will be compared using kappa statistic and correlation estimates

Beryllium Worker Responses



Respondents To Date (15 May 98): Characteristics

N = 124	YES (%)	NO (%)	Missing
Building 313 or 333	62 (50.0)	38 (30.6)	20 (16.1)
Reports Be Exposure	94 (75.8)	30 (24.2)	-
Be Samples Measured	18 (14.5)	38 (30.6)	68 (54.8)
Chronic Cough	37 (29.8)	15 (12.1)	29 (23.4)
Atopy	36 (29.0)	76 (61.3)	10 (8.1)
Ever Smoker	72 (58.1)	51 (41.1)	-
Blood LPT *(to be drawn)	61 (49.2)	63(50.8)*	-

Beryllium Worker Respondents To Date (15 May 98): Characteristics

AGE:

Range: 21- 86 years

Average: 62

SEX:

108 males (87.1%)

16 females (12.9%)

Beryllium Sensitive (LPT +):

1/61 1.6%

Beryllium Worker Respondents: Potentially Confounding Exposures

Exposure	YES (%)	NO (%)
Asbestos	72 (58.1)	52 (41.9)
Plutonium	65 (52.4)	59 (47.6)
Silica	43 (34.7)	81 (65.3)
Vanadium	13 (10.5)	111 (89.5)
Titanium	41 (33.1)	83 (66.9)
Cobalt	26 (21.0)	98 (79.0)

Discussion

- **Most workers with CBD require ongoing medical management. Any workers identified as beryllium sensitized or diseased would be offered referral services to specialists in qualified clinics. Repeat evaluation for all exposed workers every 3 years is an appropriate interval for re-evaluation for all patients with a history of beryllium exposure.**
- **Some beryllium workers develop persistently abnormal LPT and no evidence of beryllium disease. This may be due to a variable latency period between sensitization and development of disease, or variability in individual sensitivity to exposure.**
- **The natural history of beryllium sensitization after beryllium exposure and of CBD after sensitization remains to be defined by a longitudinal study. Similarly, the efficacy of early identification in reducing the morbidity of chronic beryllium disease requires a controlled clinical trial. By identifying and following large numbers of US DOE workers in a registry, such studies will be possible.**

Future Plans

- Study the population of workers who will be involved in the decommissioning of Buildings 313 and 333 and other beryllium contaminated facilities. This study would include a detailed exposure assessment of workers along with medical surveillance in order to investigate a potential exposure-response relationship between beryllium exposure and sensitization. Because CBD is an immunologically-mediated disease and exposure measures are crude estimates of biologically available dose, this relationship is skewed (4). Longitudinal studies will be required to reveal the natural history of the disease. Job task and/or form of beryllium used may prove to be a better predictor of disease outcome.

Future Plans

- Pool the results of this study with the results of other studies of sensitization prevalence, including information on current workers at Hanford, over 200 of which have a history of past exposures, existing data from Oak Ridge, Fernald, Los Alamos and Rocky Flats to provide the US DOE with a more accurate assessment of medical monitoring needs. Look for additional risks from asbestos and radiation and pulmonary fibrosis in this cohort.

References

1. Kriebel D, Brain JD, Sprince NL, Kazemi H. The pulmonary toxicity of beryllium. American Review of Respiratory Disease, 1988; 137:464-473.
2. Morgan WKC. Berylliosis. In Morgan WKD, Seaton A, ed. Occupational Lung Disease. Philadelphia: WB Saunders, 1995.
3. Kreiss K, Newman LS, Mroz MM, Campbell, PA. Screening blood test identifies subclinical beryllium disease. Journal of Occupational Medicine, 1989; 31:603-608.
4. Kreiss K, Mroz MM, Zhen B, Martyny JW, and Newman LS. Epidemiology of beryllium sensitization and disease in nuclear workers. American Review of Respiratory Disease, 1993; 148:985-997.
5. Kreiss K, Mroz MM, Wasserman S, Newman LS. Beryllium disease screening in the ceramics industry. Journal of Occupational Medicine, 1993; 35:274-276.
6. Newman LS and Kreiss K. Nonoccupational beryllium disease masquerading as sarcoidosis: Identification by blood lymphocyte proliferation response to beryllium. American Review of Respiratory Disease, 1992; 145:1212-1214
7. Markham TN. Pulmonary Function Testing. In Rossman MD, Preuss OP, Powers MB, eds. Beryllium-Biomedical and Environmental Aspects. Williams & Wilkins, 1991: 193-199.